

Appl. No. 09/848,249
Reply to Office action of June 5, 2003

Remarks

As a preliminary matter, applicant acknowledges that claims 18 and 19 are free from the prior art, and that these claims have only been objected to as being dependent upon a rejected base claim. Claims 18 and 19 have been rewritten in independent form as claims 24 and 25, respectively.

Claims 1, 2, 4-13, and 15-23 were pending. By way of this response, claims 1, 2, 10, 11, 15, 16, 18, 19, 22, and 23 have been amended, and claims 24 and 25 have been added. Support for the amendments to the specification and the claims can be found in the application as originally filed, and no new matter has been added. Accordingly, claims 1, 2, 4-13, and 15-25 are currently pending. Applicant respectfully requests entry of this amendment and reconsideration of the rejections.

Rejection Under 35 U.S.C. § 102

Claims 1, 2, 4-6, 14-17 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Neumann. Claims 1, 2, 5, 6, 9-13, 15-17, and 20-21 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by DeSantis Jr. et al.

Although applicant disagrees with the rejections, claim 1 has been amended as set forth above. Claim 1, and the claims dependent therefrom, recite that the composition not only includes a quinoxaline component complexed with a fatty acid component to enhance movement across a lipid membrane, but also that the composition results in a reduction of at least one

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undesirable side effect when the composition is administered to a patient relative to a substantially identical composition containing a quinoxaline component without a fatty acid component. Applicant respectfully traverses the rejections as they relate to the amended claims.

Applicant submits that not only does the prior art fail to teach compositions comprising a complex of a quinoxaline component and a fatty acid component which results in enhanced movement of the quinoxaline component across lipid membranes, but the prior art also fails to teach, disclose, or even suggest a composition comprising such a complex that also results in a reduction of at least one undesirable side effect when administered to a patient, relative to a substantially identical composition containing a quinoxaline component without a fatty acid component. Accordingly, applicant submits that the present claims, that is claims 1, 2, 4-6, 9-13, and 14-17 are not anticipated by the prior art under 35 U.S.C. § 102.

The Office Action states that it is inherent that the prior art compositions form complexes (page 2, last paragraph). The Office Action also states that the prior art teaches the fatty acid concentration within the range of the claimed invention. Applicant respectfully disagrees.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." (Emphasis added; *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). When a reference is used to anticipate a claim and the reference is silent about the

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asserted inherent characteristic, extrinsic evidence may be used to fill that gap. "Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference ..." *Continental Can Co. USA Inc. v. Monsanto Co.* 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749-50 (Fed. Cir. 1991) (emphasis added). "Inherency may not be established by probabilities or possibilities." *Scaltech Inc. v. Retec/Tetra L.L.C.* 178 F.3d 1378, 1384, 51 USPQ2d 1055, 1059 (Fed. Cir. 1999) (emphasis added).

Also, applicant respectfully submits that the Examiner has not established a *prima facie* case of anticipation. As indicated above, claims can be anticipated if, and only if, a single prior art reference expressly or inherently discloses each and every element recited in the claims.

Applicant respectfully requests the Examiner to precisely indicate where (by column and line number) each and every element of the pending claims is expressly or inherently disclosed in Neumann and DeSantis Jr. et al. Specifically, applicant requests the Examiner to indicate where either reference discloses a complex between a quinoxaline component and a fatty acid component, and where either reference discloses the claimed ranges.

If necessary, and pursuant to 37 C.F.R. § 1.104(d)(2), applicant respectfully requests the Examiner to provide a reference with support from an affidavit showing that complexes necessarily form when mixing pharmaceutical components. Absent such a showing, applicant submits that the present rejections cannot be maintained, and must be withdrawn.

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Applicant submits that neither Neumann nor DeSantis Jr. et al. specifically expressly or inherently disclose a composition that comprises a quinoxaline component complexed with a fatty acid component, let alone a composition which is effective to reduce at least one undesirable side effect when administered to a patient relative to a composition without the fatty acid component, as recited in the present claims. For example, Neumann discloses the use of magnesium stearate and stearic acid as pharmaceutically inert lubricants (column 3, lines 13-25). Lubricants used in tablet formation, as disclosed by Neumann, do not form complexes with the therapeutic components in tablet compositions.

As understood by persons of ordinary skill in the art, in tablet manufacturing, lubricants, such as magnesium stearate and stearic acid, are required to ensure that the tableting powder (i.e., the raw ingredient blend) does not stick to the pressing equipment. Lubricants improve the flow of powder mixes through the presses, and they help finished tablets release from the equipment with reduced friction and breakage (see the attached Exhibit A, USANA® Technical Bulletin, published May 1998). Accordingly, Neumann clearly discloses the use of stearic acid and magnesium stearate as lubricants used in the manufacture of tablets, and Neumann does not disclose the stearic acid being present in a complex with a quinoxaline component, let alone in an amount that enhances movement of the quinoxaline component across a lipid membrane.

Absent such express or inherent disclosure, the references cannot properly be used to anticipate the claimed invention, and

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the rejection must be withdrawn. In addition, applicant submits that neither Neuman nor DeSantis Jr. et al. alone or in combination provides even a suggestion to modify the reference or references to obtain the claimed invention.

In view of the above, applicant submits that the present claims 1, 2, 4-6, 9-13, and 14-17 are not anticipated by, and are unobvious from and patentable over, Neumann and DeSantis Jr. et al. under 35 U.S.C. §§ 102 and 103.

Rejections Under 35 U.S.C. § 103

Claims 7, 8, 22, and 23 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over WO 00/44355. Applicant traverses the rejections.

It is the Examiner's position that, based on the disclosure of WO 00/44355, it would have been obvious to a person skilled in the art to substitute one fatty acid or alpha-2-adrenergic agonist for another, absent of evidence to the contrary. (November 5, 2002 Office Action, page 3). Applicant respectfully disagrees and respectfully submits that the Examiner's position is not the proper legal standard on which an obviousness rejection is made under 35 U.S.C. § 103.

As applicant indicated previously, WO 00/44355 actually teaches away from the presently claimed compositions since WO 00/44355 is directed to low solubility salts. In contrast, the presently claimed compositions are directed to complexes including a fatty acid component that is effective to enhance movement of a quinoxaline component across a lipid membrane.

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"As a general rule, references that teach away cannot serve to create a prima facie case of obviousness." (*McGinley v. Franklin Sports, Inc.* CAFC 8/21/01 citing *In re Gurley*, 31 USPQ2d 1131, (Fed. Cir. 1994)). Accordingly, because WO 00/44355 is directed to low solubility salts, and because the present invention is directed to compositions containing a quinoxaline component with enhanced movement properties, applicant submits that one of ordinary skill in the art would not be motivated to modify WO 00/44355 to obtain the present invention.

In addition, as stated in the application, and as recited in the present claims, the present compositions result in the unexpected advantage of the reduction of at least one undesirable side effect when the composition is administered to a patient, relative to a substantially identical composition without a fatty acid component. Applicant submits that WO 00/44355 does not disclose, teach, or even suggest the present claims, and does not provide any motivation to one of ordinary skill in the art to extend the different teachings of WO 00/44355 to obtain the present invention.

Furthermore, even if a motivation were present to modify WO 00/44355, which applicant does not concede, the modification would fail to disclose, teach, or even suggest all of the claim limitations, including for example, a complex between a quinoxaline component and a fatty acid component, and the reduction of at least one undesirable side effect when the composition is administered to a patient.

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In view of the above, applicant submits that the present claims, and in particular claims 7, 8, 22, and 23, are unobvious from and patentable over WO 00/44355 under 35 U.S.C. § 103.

In addition, applicant submits that each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present compositions including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

In conclusion, applicant has shown that the present claims are not anticipated by and are unobvious from and patentable over the prior art under 35 U.S.C. §§ 102 and 103. Therefore, applicant submits that the present claims, that is claims 1, 2, 4-13, and 15-25 are allowable. Applicant respectfully requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Date: AUGUST 5, 2003

Respectfully submitted,



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EXHIBIT A

USANA® Technical Bulletin

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Tablet Excipients

Technical Background

Excipients are inactive, non-medicinal ingredients that are used by all manufacturers of tableted products to impart desirable characteristics important for manufacture, convenience of use, and product efficacy. Most are powdered materials that are blended with the active ingredients prior to tableting. Excipients may be classified as follows according to their general function.

- **Binders** are added to hold a tablet together after it has been compressed. Without binders, tablets would break down into their component powders during packaging, shipping, and routine handling.
- **Disintegrants** are used to ensure that, when a tablet is ingested, it breaks down in the stomach quickly into its fine powder form. Rapid disintegration is a necessary first step in ensuring that the active ingredients are bioavailable and readily absorbed.
- **Lubricants** are required during manufacture to ensure that the tableting powder (i.e. the raw ingredient blend) does not stick to the pressing equipment. Lubricants improve the flow of powder mixes through the presses, and they help finished tablets release from the equipment with a minimum of friction and breakage.
- **Sweetening and Flavoring Agents** are commonly added to chewable tablet formulations to improve taste, texture and overall palatability.
- **Coating Agents** are used to impart a finished look and a smooth surface to tablets, and to mask any unpleasant flavors that the tablet ingredients may have. Coating agents are applied after tablet pressing in a separate operation.
- **Emulsifying agents** are widely used as dispersing, suspending and clarifying agents. They are used to stabilize blends of liquids that are not mutually soluble and improve the bioavailability of some lipid-soluble compounds.

Excipients Used in USANA's Nutritional Tablets

Several excipients are used in USANA tablet formulations. They are selected for their inertness, non-toxicity and contribution to the overall integrity and performance of the product. All have excellent safety profiles and meet the requirements of the U.S. Pharmacopeia guidelines. Many serve multiple functions (e.g. disintegrant and binder). All are "high performance" meaning that minimal amounts can be added to achieve the desired effects. Descriptions of each follow.

- **Starch and Pregelatinized Starch** are used primarily as binders to improve tablet durability and integrity. Both are derived from corn. Pregelatinized starch is partially

hydrolyzed and dried to make it flow better during tableting. It also has superior binding characteristics. Starch and pregelatinized starch are also used as disintegrants. After ingestion, these starch granules swell in the fluid environment of the stomach and force the tablet to break apart.

- **Microcrystalline Cellulose** serves multiple functions in tablet formulas. It is an excellent binder and disintegrant. It is derived from plant fiber.
- **Croscarmellose Sodium** is called a "super disintegrant" because it is very effective even at very low concentrations at promoting the breakdown of tablets following ingestion. It is manufactured from cellulose (plant fiber) which has been processed to have a high affinity for water.
- **Fumed Silica** is an extremely fine form of silicon dioxide. (Silicon dioxide occurs naturally as quartz or sand.) It is a white powdery material that is used in formulations to promote flow of tableting powders and to prevent their sticking in tablet presses. It also promotes tablet disintegration.
- **Talc**, a natural magnesium silicate mineral, is a fine white powder that, like fumed silica, is used as a tableting lubricant and flow agent.
- **Ascorbyl Palmitate** is used primarily as a lubricant to improve the flow of tableting powders in the presses during manufacture and to facilitate ejection of tablets from the equipment following compression. While more costly than standard lubricants, ascorbyl palmitate, which is a fat-soluble form of vitamin C, also provides some additional vitamin C activity.
- **Fructose and Mannitol** are used in Kids Chooables as sweetening agents to mask the unpleasant taste of vitamins and help improve the texture. Both are natural sweeteners extracted and purified from plant sources, particularly from fruits. In addition, these ingredients have good binding properties and aid in tablet formation and integrity.
- **Hydroxypropyl Methylcellulose** is used as a film-coating agent on all USANA tablets except Kids Choo-ables. As its name implies, this excipient is derived from cellulose or plant fiber.
- **Carnauba Wax** is a constituent of the film-coating agent on all USANA tablets except Kids Chooables. It is a natural wax which helps protect the tablets and aids in the ease of swallowing the tablets.
- **Maltodextrin**, which is derived from the partial hydrolysis of starch, is another constituent of the film-coating agent on all USANA tablets except Kids Chooables.
- **Polysorbate 80, Polyethylene Glycol 400, Propylene Glycol, Sorbitan-Monooleate, and Pladone** function as lipophilic emulsifiers, stabilizers and suspending agents to improve the solubility of CoQ10 in USANA's CoQuinone. These ingredients are commonly used in the pharmaceutical industry in over-the-counter and prescription medicines, in the cosmetic industry in thousands of cosmetic products, and in the food industry as components of beverages, baked goods and frozen desserts. All have well documented long-term safety profiles and pose no health hazard at the levels used for such products under conditions of good manufacturing practice.